MENDED CLAP20 Rec'd PCV/FIO 08 MAR 2006

[received by the International Bureau on 31 August 2005 (31.08.2005); Original claims 1-75 are replaced by Amended Claims 1-75]

Formula IV

wherein:

R₇ is anyl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl; and

R₈ and R₉ are the same or different and are each hydrocarbyl, optionally substituted with one or more halogens or lower alkyl groups, or

R₈ and R₉ together form a heterocyclic ring having five, six or seven atoms, including the intervening nitrogen and optionally containing other heteroatoms, and also optionally substituted with one or more halogens or lower alkyl groups;

$$R_{11}$$
 Formula V

wherein

10 K is as defined above; and

R₁₀ and R₁₁ are the same or different and each is an aryl group, optionally substituted with a second aryl group that may be the same or different and the aryl groups may be substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl;

$$\begin{array}{c}
M_1 \\
M_2 \\
N
\end{array}$$

$$\begin{array}{c}
R_{12} \\
N
\end{array}$$

Formula VI

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wherein:

p is an integer from 1-3;

M₁, M₂, and M₃ are the same or different and each is S or O;

Z is S, & or P;

R is hydrocarbyl or OR35, where R35 is H or hydrocarbyl; and

 R_{12} and R_{13} are the same or different and each is hydrocarbyl, a heterocyclic ring or lower alkyl, or R_{12} and R_{13} together form a ring;

wherein:

K is as defined above;

r is and integer from 1-3;

R₁₄ and R₁₅ are the same or different and each is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen, a heterocyclic ring and hydrocarbyl; and

5 R₁₆ and R₁₇ are the same or different and each is hydrocarbyl or a hetercyclic ring;

Formula VIII

wherein:

s is an integer from 1-10;

R₂₀, R₂₁, R₂₂ and R₂₃ are the same or different and each is H, aryl, optionally substituted with one or more halogen or lower alkyl groups, hydrocarbyl and a heterocyclic ring; and

10 R₁₈, R₁₉ are the same or different and each is anyl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen and lower alkyl;

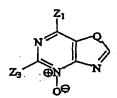
Formula XII

wherein:

t is an integer from 1-5;

u is an integer from 1-2; and

15 R₂₄ is selected from H, a heteroyc lic ring and hydrocarbyl, optionally substituted by halogen; and



Formula XIII

wherein:

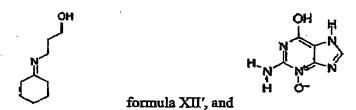
Q is selected from CH2, NH, S and O; and

Z₁ and Z₃ are the same or different and selected from CH₃, NH₂, OH and SH.

20 or tautomers thereof.

2. The complex of claim 1, wherein the compound is selected from

formula XI',



formula XIII',

- 5 or a pharmaceutically acceptable salt thereof.
 - 3. The complex of claim 1, which is in an animal.
 - 4. The complex of claim 1, which is in vitro.

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5. A complex comprising a compound of one of

wherein:

v is an integer from 1-3; and

G₁ and G₂ are the same or different and each is selected from CH₂, NH, S and O;

$$R_{28}$$
 OH R_{25} or the corresponding quinone R_{28} R_{27}

15 Formula XVI

wherein:

R₂₅, R₂₆, R₂₇, and R₂₈ are the same or different and each is selected from halogen and hydrocarbyl, particularly lower alkyl; and

$$R_{29}$$
 N=0 Formula XVII

wherein:

K is as defined above, and

R₂₉ and R₃₀ are the same or different and each is aryl optionally substituted with one or more groups selected from -OH, -NH₂, -SH, halogen and hydrocarbyl;

- 5 in association with a gastric releasing peptide (GRP).
 - 6. The complex of claim 5, wherein the compound is of one of

Formula XIV',

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Formula XVI', or

Formula XVII'.

- 7. The complex of claim 5, which is in an animal (e.g., a mammal).
 - 8. The complex of claim 5, which is in vitro.
- 9. A pharmaceutical composition comprising a compound of one of formula I VIII, XII, or XIII
 15 as defined in claim 1, or one of formula XIV, XVI or XVII as defined in claim 5, and a
 pharmaceutically acceptable carrier.
 - 10. The pharmaceutical composition of claim 9, wherein the compound is of one of formula I'-XIII' as defined in claim 2, or one of formula XIV', XVI', or XVII' as defined in claim 6.
 - 11. A method for inhibiting an activity of an AM peptide, comprising contacting the peptide with an effective amount of a compound of one of formula I VII as defined in claim 1.
- 12. The method of claim 11, wherein the compound is of one of formula I' VII', as defined in claim 2.

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said compound(s) and a pharmaceutically acceptable carrier, and, optionally, a container or packaging material.

- 54. The kit of claim 53, wherein the compound(s) is selected from formula I' through XIII', as defined in claim 2.
 - 55. A kit suitable for treating a subject suffering from a condition mediated by an aberrant expression and/or activity of gastrin releasing peptide (GRP), comprising one or more of the compounds of formula XIV, XVI or XVII, as defined in claim 5, or a pharmaceutical composition comprising said compound(s) and a pharmaceutically acceptable carrier, and, optionally, a container or packaging material.
 - 56. The kit of claim 55, wherein the compound(s) is of one of formula XIV', XVI' and/or XVII', as defined in claim 6.

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- 57. A kit suitable for detecting an AM peptide, comprising
- a) one or more compounds selected from formula I VIII, XII or XIII, as defined in claim 1, which is detectably labeled, and, optionally,
 - b) means to detect the labeled compound associated with (bound to) the peptide.

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- 58. The kit of claim 57, wherein the compound(s) is of one of formula I' XIII', as defined in claim 2.
- 59. A kit suitable for detecting a GRP peptide, comprising

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- a) one or more compounds selected from formula XIV, XVI, XVII, as defined in claim 5 and XV, as defined in claim 49, which is detectably labeled, and, optionally,
 - b) means to detect the labeled compound associated with (bound to) the peptide.
- 60. The kit of claim 59, wherein the compound(s) is selected from formula XIV', XVI', XVII', as defined in claim 6 and XV', as defined in claim 50.
 - 61. A kit of claim 53 or 55, wherein said compound is in a pharmaceutically acceptable carrier.

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62. A method for inhibiting GRP-mediated angiogenesis in a subject in need of such treatment, comprising administering to the subject an effective amount of an agent that inhibits GRP,

provided that the GRP-mediated angiogenesis is not angiogenesis involved in tumor growth or metastasis.

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63. A method for preventing or treating condition mediated by GRP-mediated angiogenesis in a subject in need of such treatment, comprising administering to the subject an effective amount of an agent that inhibits GRP,

provided that the condition is not angiogenesis dependent tumor growth.

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64. A method for preventing or treating one of the following angiogenesis-mediated conditions in a subject:

arthritis (e.g, rheumatoid arthritis),

psoriasis,

benign growths caused by rapidly dividing cells,

brain ischaemia.

vascular diseases.

ocular diseases involving ocular neovascularization or related ocular diseases and disorders,

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fibrosis,

deep venous thrombosis,

endometriosis, or

wrinkles,

comprising administering to the subject an effective amount of an agent that inhibits

25 GRP.

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65. A method for inhibiting angiogenesis-mediated tumor growth in a subject in need of such treatment, comprising

administering to the subject an effective amount of an agent that inhibits GRP, and detecting or monitoring the reduction in blood vessels (inhibition of angiogenesis).

66. The method of claim 62, wherein the agent is a compound of formula XV as defined in claim 49.

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67. The method of claim 63, wherein the agent is a compound of formula XV as defined in claim 49.

68. The method of claim 64, wherein the agent is a compound of formula XV as defined in claim 49.

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- 69. The method of claim 65, wherein the agent is a compound of formula XV as defined in claim 49.
- 70. The method of claim 62, wherein the agent is a compound of formula XV' as defined in claim 50.
 - 71. The method of claim 63, wherein the agent is a compound of formula XV' as defined in claim 50.
- 72. The method of claim 64, wherein the agent is a compound of formula XV' as defined in claim 50.
- 73. The method of claim 65, wherein the agent is a compound of formula XV' as defined in claim 50.
 - 74. A method for treating low blood pressure or an eating disorder in a subject in need of such treatment, comprising administering to the subject an effective amount of a compound of formula XV as defined in claim 49.
 - 75. The method of claim 74, wherein the compound is of formula XV as defined in claim 50.



Statement Under Article 19(1)

The claims have been amended in response to comments in the Written Opinion mailed 1 July 2005 in the above-referenced application. The following pages show the specific amendments made to the various claims.

Explanation of Amendments

In claim 1, formula VII has been amended to correct an obvious error. A correction to this formula under Rule 91 is being submitted concurrently with this amendment. Also, the definition of the variables R18 and R19 of formula VIII is clarified by the substitution of "and" for "or."

In claim 5, the variable G_3 in the definition of formula XIV is replaced by G_2 . Claims 6, 7 and 8 now depend from claim 5.

Claim 9 refers to claim 1 with regard to formulas I-VIII, XII and XIII, and to claim 5 with regard to formulas XIV, XVI and XVII.

Claim 10 refers to claim 2 with regard to formulas F-XIIF, and to claim 6 with regard to formulas XIV', XVI' and XVII'.

Claim 60 now depends from claim 59.

Claim 61 no longer recites a preamble.

Claim 64 no longer recites "(e.g., noncancerous melanomas)"

Applicant submits that the amended claims address certain points raised by the Examiner in the Written Opinion.